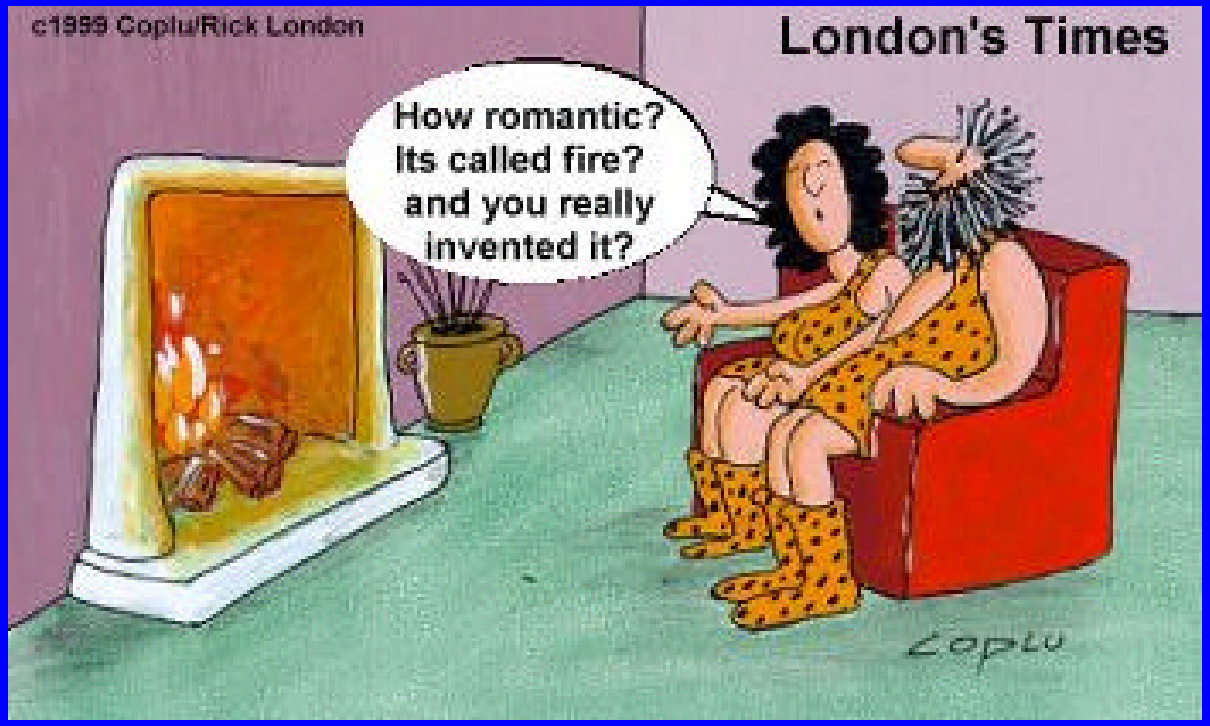
CBER 2005 Update-
Innovation & Public Health



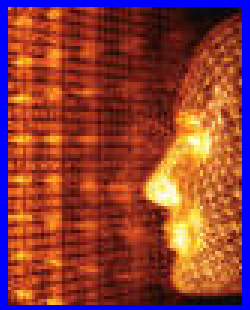
Update for WCBP

Jesse L. Goodman MD, MPH

January 10. 2005

Overview

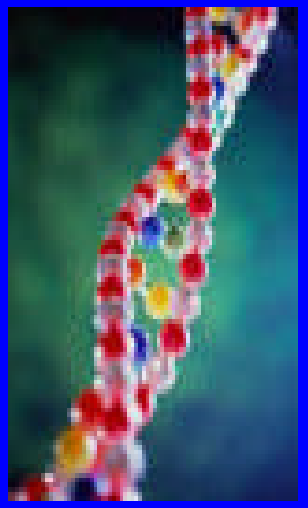
- **Take stock of some of the year's accomplishments**
- **Provide updates on progress in ongoing Center and Agency efforts**
- **New initiatives**
- **Standards activities and potential opportunities of interest to WCBP**



Vision for CBER

INNOVATIVE TECHNOLOGY ADVANCING PUBLIC HEALTH

- ***Protect and improve public and individual health in the US and, where feasible, globally***
- ***Facilitate the development, approval and access to safe and effective products and promising new technologies***
- ***Strengthen CBER as a preeminent regulatory organization for biologics***

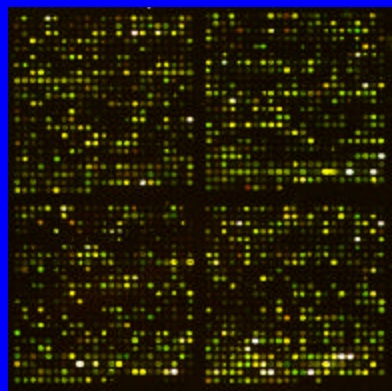


Selected Accomplishments

- **Product Review:**
  - **Continue to meet PDUFA & MDUFMA milestones for actions**
  - **Public Health**
    - **Influenza:**
      - **Vaccine shortage: Chiron remediation, INDs**
      - **Pandemic preparedness:**
        - » **Key role including in HHS preparedness plan issued 8/04**
        - » **Assisting in landmark collaborative effort to produce H5N1 vaccine (manufacturing, reagents etc.)**
        - » **Enhance manufacturing capacity, more licensed vaccines**
    - **WNV: continuing success of blood screening**
    - **Continued phase in of thimerosal reduced/free vaccines**
    - **Significant approvals: e.g. OraQuick, FVIII**

Selected Accomplishments II.

- **Patient Safety**
  - **Joint CBER/CDER risk, pharmacovigilance and data monitoring committee guidances**
  - **Continuing vaccine safety CMS collab.: increase use of large databases**
  - **VAERS data-mining projects**
- **New Technologies**
  - **Outreach and policy: BRMACs on cord blood, islet cell and cell Rx for cardiac disease**
  - **Gene therapy long term follow up meeting & planned guidance**
  - **Cancer vaccines into Phase III**
  - **Work on microarray standards, genomics guidances, proteomics etc.**



Selected Accomplishments III.

- **IT:**
  - **e-labeling, barcode rules**
  - **EDR, VAERS, CBAERS enhancements**
    - **Allow faster AE reporting**
- **Communications and Outreach:**
  - **HIV vaccine meetings**
  - **Workshops including**
    - **CT Product Development**
    - **Anthrax therapeutics (joint with CDER)**
    - **Plasma standards**
    - **Bayesian and adaptive trial designs**
  - **Initiation of Manufacturing/Blood Banking Site Visit Program**

Selected Accomplishments IV.

- **International Efforts**
  - **Re-designated WHO Collaborating Center**
  - **Leadership efforts with WHO/HHS on pandemic flu**
  - **New MOUs: EU, Canada, Switzerland: current priority to assess, extend and broaden**
  - **Xeno and Gene therapy outreach with WHO, others**
  - **GCBS leadership**
  - **ICH (including GT) , PICS**
  - **ICDRA**

Update on CBER 2004 Strategic Initiatives

- **Enhanced Review Management and Processes**
  - **Monthly review management updates**
- ***Review Template Initiative***
  - ***Enhance consistency, quality of review and submissions and facilitate electronic processes***
  - Progress to date on templates:
    - **Clinical: IND and BLA templates near ready**
    - **Pharm tox: building on modified ODE VI template**
    - **CMC, Statistical: under review**

CBER 2004-5 Initiatives Update II

- GMPs for 21st Century –
  - Guidances and reports rolled out
  - CBER using many practices endorsed by FDA
    - e.g.: scientists/clinicians on inspections, specialized teams & training, risk based prioritization
    - New system-based, risk-based compliance programs issued: plasma and biologics
  - "Specifications for Biological and Biotechnological Products" Joint public workshop with CDER and AAPS
  - For 2005: Pharmaceutical Quality Council: to further implement

Process Analytical Technologies

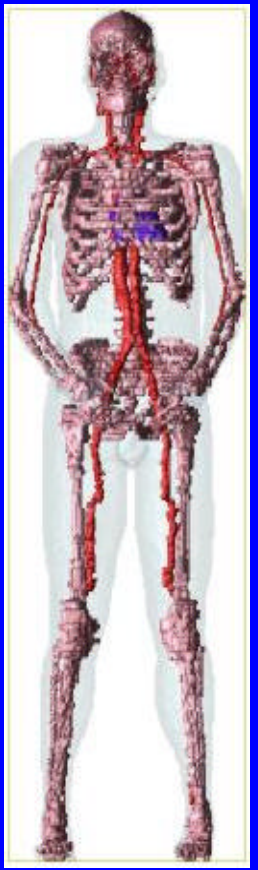
- CBER continues to encourage manufacturing and testing innovation and improvement
  - CBER is participating as an observer on the FDA PAT group to facilitate information sharing on approaches and technical issues
- Implementation of PAT will occur through integrated system of review and inspection
- Lessons learned from the Team Biologics program, particularly the more recent inclusion of Quality Systems, will be used by the PAT Team and the Pharmaceutical Inspectorate.

Rapid Microbial Testing

- ***Rapid Microbial Methods***
- CBER seminar series in 2003 – 2004
  - outside speakers including developers of different technology discussed various methods and associated technology issues
- Active in-house research on developing and assessing rapid methods for bioburden/ sterility and mycoplasma detection
- Recently (August 2003 and February 2004) approved rapid microbial methods for use with cellular products.

2004 Initiatives Update III.

- **Patient Safety- Tissues**
  - **Tissue Safety Framework**
    - **Finalization of Donor Suitability & GTP Rules: DONE!**
    - **Adverse Event Reports and Analysis**
      - **Active Surveillance as one ultimate goal: resources**
    - **Training, outreach, inspection and compliance**
  - **Tissue Safety Team formed including OCTGT, OCBQ, OBE, OCTMA, OBRR and IOD**
    - **Developing SOPs to facilitate reporting/receipt/investigation of AEs**
    - **Development of shared databases and drive(s)**
    - **Liaison with ORA, CDC, and HRSA**



CBER 2004 Initiatives Update IV

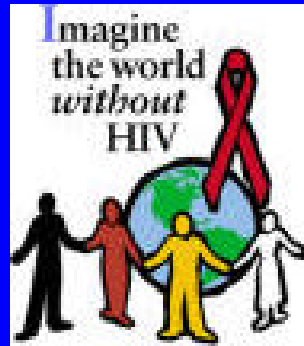
- *Strong FDA*
  - **Reorganization/Refocusing and streamlining of Director's and Management Offices**
  - **Review Management and QA relocated with review**
  - **Enhanced Emergency Response Capabilities**
  - **Training/professional development**
    - **New 2 day Risk Assessment Course for Reviewers successfully inaugurated 9/04 (collaboration with Virginia Tech)**
    - **Risk Management course - quantitative focus**
    - **Risk Communication module also inaugurated**

CBER 2004: Update on Major Initiatives V.

- Counterterrorism
  - FDA and CBER information on product security for manufacturers
  - Spore former guidance: increases flexibility, reduces costs
  - EUA law & draft guidance
  - New approaches to product labeling for strategic stockpile
  - Progress in SPx and anthrax vaccines, immunoglobulin development/review
    - Successful management/communication re: SPX vaccine cardiac AEs
    - Baby BIG approval, VIG availability and BLA submission

CBER 2004: Update on Major Initiatives VII.

- **Global Vaccine Assistance**
  - **March, 2004 PAHO meeting: opportunities for increased training and technical consultation**
  - **Increasing focus on harmonization, e.g., w/EMEA; encourage global vaccine development plans**



2005: Building on Success- Major Strategic Initiatives

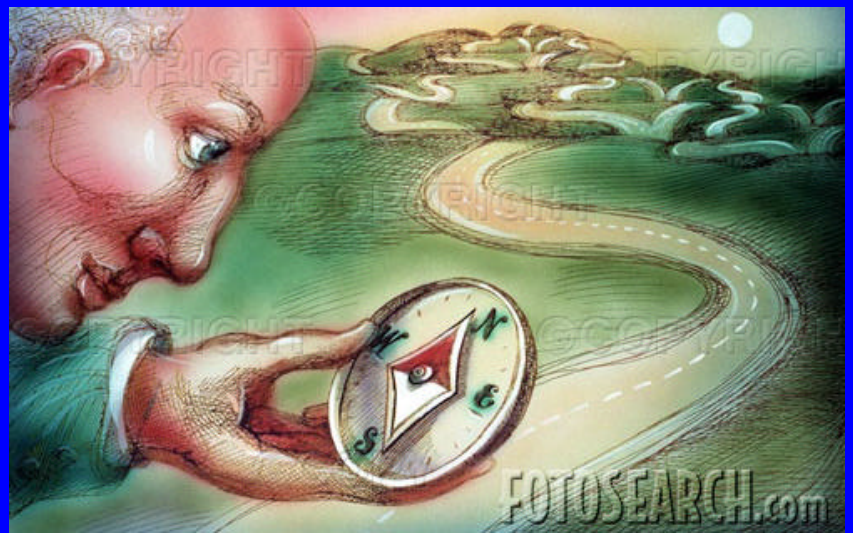
- ***I. Critical Path*** **– Agency-wide**
  - **Identify, focus upon and manage to regulatory and scientific opportunities to improve product development process and availability of needed products**
    - **Intramural and extramural research**
    - **Needed policy and guidance**
  - **Opportunity to promote and preserve a science based FDA**
  - **High level CBER Research Working Group formed and evaluating organization: to present options**

Recent CBER Collaborative Science Supporting Innovation

- **Potency/effectiveness/standards**
  - **High throughput smallpox Ab/VIG potency assay**
  - **International Factor, thrombin, adenovirus standards**
  - **Proteomic monitoring of cancer treatment**
  - **Surrogate markers/models of efficacy; TB, tularemia, hepC, pneumococcus, IGIV**
  - **Embryonic stem cell gene expression**
- **Safety**
  - **West Nile testing standards and reagents**
  - **Vaccine/cell safety and adventitious agent tests (e.g. PERT, PERV, TSE)**
  - **Gene Rx , endothelial cell predictive toxicity models**
  - **Oxidative toxicity of RBC substitutes link to structure/chemistry**
- **Consistency/manufacturing/quality**
  - **Conjugate vaccine synthesis methods**
  - **Prion inactivation and testing**
  - **Influenza seed strains, reassortants, stds & methods**

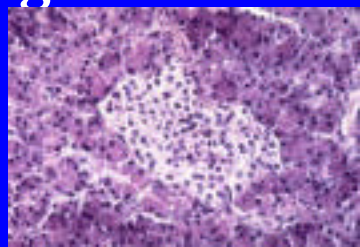
Critical Path: continued

- **Seeking input in identifying opportunities, collaborators and priorities**
  - **CBER October CP Stakeholders mtg: 200 people!**
  - **AC presentations**
- **Providing content and perspective for our product and cross-cutting offices**



Examples of CBER Critical Path Investment Opportunities

- Develop/make available well characterized cell banks (and methods to assay for safety/adventitious agents) for vaccine and biologics production – & update guidance
- Characterization of cell therapies & links to standardized clinical/lab outcomes (e.g. HPSCs)
- New assays, standards, biomarkers, surrogates for complex biologics safety, efficacy and quality- WCBP
- Methods & validation of pathogen inactivation for blood, plasma, tissues and other products
- Multipathogen and rapid detection methodologies
- Improving longevity/storage of blood/tissues
- Enhanced clinical trial design/analysis



Selected CBER Standards Activities

- In FY 2004, over 35 CBER staff participated with over 20 separate organizations to develop standards for use in product testing
- Broad representation including international and national organizations (e.g., WHO, PAHO, ICH) governmental organizations (e.g., NIST, NIH, CDC), regulated industry groups and other interested parties

Examples Standards Activities

- ICH - Harmonization of pharmacopoeial methods - examples include methods for sterility, endotoxin, and extractable volume
- WHO working group - International Reference Preparations for HBsAg and anti-HCV Diagnostic Kits - Assessment of the candidate HBsAg International Standard and Reference Panel, and discussion on the feasibility of an International anti-HCV monospecific Reference Panel.

Examples Standards Activities

- NIST/ NIH/ CDC - Flow cytometry calibration standards & guideline on Identifying the Optimal Methods for Clinical Quantitative Flow Cytometry
- External RNA Controls Consortium/ National Committee for Clinical Laboratory Standards - Development of RNA spike-in controls for use in microarray and RT-PCR experiments, associated guideline for use

Examples Standards Activities

- WHO – developing and standardizing Pertussis Reference Antiserum; revising guidelines for Diphtheria, Tetanus, Pertussis and Combined Vaccines - potency testing of diphtheria and tetanus vaccines
- WHO - Standardized BCG preparation and a TB challenge strain to create a tuberculosis vaccine testing model
- EDQM/ EP – participating in collaborative study of replacement serological methods for potency testing of diphtheria toxoid vaccines

Examples Standards Activities

- AABB, FACCT, NMDP, ARC, ISCT jointly drafting Hematopoietic Progenitor Cell Product Circular of Information
- Multiple companies and groups - Adenovirus-Associated Vector (AAV) Reference Standard Working Group – developing and assessing AAV reference standard stock for use in normalization of titers for recombinant AAV vectors across clinical trials using AAV.

Examples of Standards Activities

- Developing and evaluating new and replacement international standards for protein blood products.
- EDQM, European Pharmacopoeia Commission Group of Experts 6B- harmonize analytical assay methods & potency standards
- PAHO/WHO Collaborating Center - potency standards for Factor IIa and VIII, and VWF
- International Society Thrombosis & Hemostasis potency standards

Evolving Science: Standards and Assays Needed

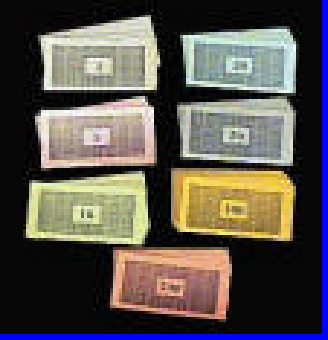
- Vaccine efficacy (e.g. flu)
- Gene therapies and DNA vaccines
- Cellular therapies (e.g. characterization of stem cells, islet cells, cardiac cells, cord blood)
- Therapeutic vaccines (assays, standards, and surrogates)
- Meaningful immunogenicity predictors

Building on Success: Major Strategic Initiatives for 2005

- ***II. Management and Organizational Training and Renewal***
  - **FDA's Gallup Program Survey – opportunity for feedback and management improvement**
  - **CBER: "Human Capital Development Program"**
    - **Pilot tools for management and mentorship of review and research efforts**
    - **Enhance training opportunities**
    - **Develop up-to-date leadership training and succession plans**

Building on Success: Major Strategic Initiatives for 2005 IV.

- ***III. Pilot Test an "Expert Consultants Academy"***
  - **Goal: Provide easier and rapid access to expertise, particularly in areas of emerging science and practice. Consultants individually available to provide input/information and, when needed, inform difficult decisions.**
  - **Existing SGE's; appoint additional experts to create online database**
  - **Possible pilots: tissues, gene therapy**
  - **Challenges: resources, COI, confidentiality**



Budget and Personnel Updates

- **Very tight for 2005**
- **OCTGT: Dr Ed Otto recruited as Office Director, Dr. Joyce Frey Vasconcells as Deputy**
- **OCBQ: Mary Malarkey as new Office Director**
- **OVRR: Dr. Norman Baylor appointed Deputy**
  OBRR: Deputy Director to be named shortly
- **OVRR, OBE: Dir. searches underway**

- ***Opportunity to recognize Joyce, Jim Cohen, Norman and Bill Egan for their contributions***

Thank you!

- We are proud of our staff and the Center's role in public health, biodefense, product safety and efficacy.
- Innovative technologies demand new models, standards and assays.
- Strong science and partnerships essential
- We see a positive future with exciting challenges.
- We welcome your input & contributions, both now & in the future.